

Occasional
Paper

Alzheimer's: The Disease of the Century



INTERNATIONAL
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The International Longevity Center–USA (ILC–USA) is a not-for-profit, nonpartisan research, education, and policy organization whose mission is to help individuals and societies address longevity and population aging in positive and productive ways, and highlight older people’s productivity and contributions to their families and society as a whole.

The organization is part of a multinational research and education consortium, which includes centers in the United States, Japan, Great Britain, France, the Dominican Republic, India, Sub-Saharan Africa, and Argentina. These centers work both autonomously and collaboratively to study how greater life expectancy and increased proportions of older people impact nations around the world.

Alzheimer's: The Disease of the Century



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INTRODUCTION

Robert N. Butler, M.D.

In 1975, I became founding director of the National Institute of Aging (NIA). At that time, as is unfortunately still the case, Alzheimer's disease accounted for more than half of all nursing home patients. But the climate of research on brain disease was such that the National Institutes of Health awarded only 12 grants for the study of brain aging, and each award recipient received about \$60,000.

Drs. Robert Katzman and Robert D. Terry, pioneers in the study of Alzheimer's disease, and Katherine Bick of the Neurology Institute conceptualized what later was recognized as a catalytic symposium. Sponsored by Dr. Donald Tower, director of the National Institute of Neurological and Communicative Disorders and Stroke, Dr. Bertram Brown, director of the National Institute of Mental Health, and I at the NIA, Alzheimer's Disease: Senile Dementia and Related Disorders was held at the NIH in 1977.

I had already decided that the fledgling NIA should identify Alzheimer's disease as a national research priority and make it a household word in order to gain both private and public funding. Dr. Tower and I invited family support groups to Bethesda and urged them to establish what became the Alzheimer's Association. Many committed individuals whose family members suffered from the disease took leadership responsibility, notably Jerry Stone, Lonnie Wollin, and Princess Yasmin Aga Khan.

In 1986 the MetLife Foundation inaugurated a critically important awards program. In two decades of remarkable progress, a distinguished committee has identified with near-perfect accuracy the scientists whose critical research endeavors have advanced the field. While we do not have a cure, we do have a greater understanding of basic pathology and have well-identified targets for intervention studies.

Of equal importance is the challenge of helping families cope with this devastating illness, and we must work to establish a national affordable and humane long-term-care system. But without a cure, by 2040 an estimated 14 million people will have Alzheimer's disease. This will result in a major national caregiving and financial crisis, with devastating consequences for both family life and national productivity.

Medical scientist and author Lewis Thomas observed that Alzheimer's disease is the "disease of the century." In the essays that follow, Stanley I. Rapoport, chief of the brain physiology and metabolism section at the National Institute on Aging, presents a brief history of the progress that has been made in our understanding of this disease. Larry D. Wright, director of northwest Arkansas' Schmieding Center for Senior Health & Education, describes the dramatic impact of Alzheimer's disease on family members and on society as a whole, and offers insights into both the challenges and opportunities for caregivers.

ALZHEIMER'S DISEASE: THIRTY YEARS OF PROGRESS

Stanley I. Rapoport, M.D.

Alzheimer's disease is the major cause of dementia in the United States, with spending in the range of \$100 billion annually. It affects 5 to 7 percent of people over 65 years of age and 20 to 40 percent over 80, and is estimated to be the fourth to fifth most common cause of death in the United States.

Concerted research efforts in the clinical and basic neurosciences in the last 30 years have resulted in marked advances in our understanding of the clinical course and mechanisms of Alzheimer's disease as well as new therapeutic directions. This review provides a short history of the progress that has been made in Alzheimer's disease research during this time, and identifies some of the seminal discoveries and insights that contributed to this progress.

A Brief History

In 1907, Alois Alzheimer reported that the brain of a 55-year-old deceased woman who had a history of progressive memory loss accompanied by morbid jealousy contained high densities of plaques and silver-staining accumulations of twisted protein fragments. These fragments were located inside the brain's nerve cells. He referred to them as "neurofibrillary tangles." The dementia associated with this neuropathological picture became known as "Alzheimer's disease."

Following Alzheimer's report, neuropathologists in psychiatric and other hospital settings accumulated large sets of clinical and postmortem data from Alzheimer's disease patients. It was not until the 1970s, when the full impact of Alzheimer's disease was recognized, that its symptoms, mechanisms, risk and genetic factors, and treatment began to be seriously addressed. These data became important in distinguishing Alzheimer's disease from brain changes that are found in other dementias, such as vascular dementia.

In the last 30 years, progress on Alzheimer's disease consisted of concurrent advances in different areas of the clinical and basic neurosciences, including clinical description, neuropathology, molecular biology, cognitive assessment, brain imaging, epidemiology, genetics, and treatment. This progress was supported in part by increased funding from the National Institutes of Health (NIH), whose annual research budget grew from only \$3.9 million in 1976 to approximately \$650 million today.

Progress in Understanding Alzheimer's Disease Neuropathology

Accumulation of tangles and plaques in brain association system

In the 1970s, scientists began to understand where Alzheimer's disease affects the brain most intensely when they recognized that its characteristic neuropathology was most dense in specific brain regions. They discovered that regions least affected are in the "primary neocortex," which is on the surface of the brain and receives auditory, visual, and sensory information, or originates movement. Regions most affected are considered to integrate various functions of primary and "association" cortical areas and subcortical areas such as the hippocampus, to regulate memory, attention, and other higher thought processes. Studies suggest that the knowledge people store from events that occurred at a specific time and place is first acquired through processing in this "association system."

Early loss of synapses and their neurotransmitters in Alzheimer's disease

Nerve-to-nerve communication within the brain occurs at connections called synapses, where a neurotransmitter is released from the terminal of one nerve to activate a receptor on the other nerve. Studies of postmortem brain from patients in the early stage of Alzheimer's disease established that synapses are the first to be lost, disproportionately to loss of the nerve cells themselves. Furthermore, synaptic loss correlated most closely with the severity of dementia prior to death, emphasizing disturbed nerve-to-nerve communication as the major cause of disturbed thinking and behavior in patients.

This conclusion was supported by evidence offered in the 1980s of reduced concentrations of synaptic neurotransmitters in the Alzheimer's disease brain. The most significant neurotransmitter deficit was shown to be acetylcholine, which plays a critical role in learning and memory. After this discovery, researchers began to develop and test drugs that might enhance acetylcholine transmission.

Insights from Direct Analysis of Plaques and Tangles

A number of critical discoveries and compelling hypotheses regarding Alzheimer's disease mechanisms were derived from studying cadaver brain samples and obtaining detailed chemical and structural analyses of the senile plaques and neurofibrillary tangles originally described by Alzheimer.

Amyloid hypothesis

Amyloid is a deposit of clumps of peptides. In the mid-1980s, the material that was identified in blood vessels and in the senile plaques of the Alzheimer's disease brain was confirmed to be composed of amyloid peptides. The peptides were shown to be breakdown products of a protein substance identified as amyloid precursor protein (APP), whose gene is on chromosome 21. On this basis, and because similar amyloid accumulation was found in brains of demented patients with Down syndrome in which chromosome 21 is duplicated, it was suggested that

Alzheimer's disease arose from a mutation of the APP gene. Later studies confirmed multiple mutations in the APP gene in families prone to familial Alzheimer's disease.

Apolipoprotein E4 as risk factor

In the early 1990s, another protein, apolipoprotein E (*ApoE*), was identified in senile plaques, vascular amyloid, and neurofibrillary tangles of the Alzheimer's disease brain. The *ApoE* gene exists in three variants, called by scientists *ApoE2*, *ApoE3*, and *ApoE4*. Inheritance of the *ApoE4* variant was shown to make people more susceptible to late-onset Alzheimer's disease, whereas inheritance of the *ApoE2* variant appeared to be protective against late-onset disease.

Tau protein

It was discovered that the silver-staining neurofibrillary tangles described by Alois Alzheimer contain a protein called tau in a chemically altered state. In healthy brain, normal tau is critical to the life of the nerve cell. But in Alzheimer's disease, the chemically altered tau protein aggregates and forms filamentous tangles, which promote nerve cell death.

Neuroinflammation

Identification of inflammatory proteins and of phagocytic cells that participate in immune reactions in the Alzheimer's disease brain, together with an initial report that people treated with nonsteroidal anti-inflammatory drugs for arthritis had a reduced incidence of Alzheimer's disease, led to a proposal that inflammation of brain cells contributes to Alzheimer's disease.

Measuring Dementia and Its Presymptomatic Stages

It was recognized quite early that if a multidisciplinary effort were to succeed in diagnosing and evaluating Alzheimer's disease, and if sufficient numbers of patients were to be recruited in research settings, researchers would have to develop scales with which to measure the severity of the patient's dementia. Several such scales were developed starting in the late 1960s. This was followed by more refined cognitive tests of attention, memory, language, and visuospatial processing, which helped to better characterize the cognitive defects in individual Alzheimer's disease patients and to distinguish the patients from healthy unaffected subjects and patients with other brain diseases.

Mild cognitive impairment

The transition between healthy brain aging and Alzheimer's disease has been a subject of much concern. In the 1960s, older persons who were not clinically demented but who complained of, or had subtle memory changes, were characterized as having "benign senescent forgetfulness," which implied that normal brain aging can

involve significant memory decline. Eventually, however, the changes of benign senescent forgetfulness were seen in a more sinister light. Now such transitional subjects are classified as having “mild cognitive impairment” and are considered more likely to have presymptomatic Alzheimer’s disease.

Psychiatric symptoms and personality changes frequently occur in patients with mild cognitive impairment, and these symptoms increase the likelihood that the patient will develop Alzheimer’s disease.

Cerebrospinal fluid markers

Cerebrospinal fluid bathes the surfaces of the brain. Obtaining this fluid through a spinal tap, researchers can measure relevant substances found in the brain, which aids in diagnosis and in acquiring indirect access to brain metabolic processes. For example, in the 1980s, the Alzheimer’s disease brain was reported to have lower levels of several substances that are produced in the brain as the end products of nerve transmission. These substances were identified as acetylcholine, dopamine, and serotonin.

Currently, altered cerebrospinal fluid levels of substances relevant to Alzheimer’s disease pathology, relating to abnormal tau and amyloid peptide production, are considered highly specific in distinguishing early Alzheimer’s disease from depression, from dementia due to alcoholism, and from Parkinson’s disease.

Neuroimaging

Studies of the postmortem brain, no matter how sophisticated, do not identify early functional and structural changes in individual brain regions and their circuits or how these changes contribute to the cognitive-behavioral profile of individual Alzheimer’s disease patients. Newly introduced methods of *in vivo* brain imaging, including computer assisted tomography (CT), magnetic resonance imaging (MRI) and spectroscopy (MRS), as well as positron emission tomography (PET), have successfully addressed these issues.

Positron emission tomography for functional brain imaging (PET)

Brain glucose metabolism and blood flow are linked and reflect brain neuronal activity. In the mid-1970s, PET scanning began to be used to quantitatively image regional cerebral metabolic rates for glucose and regional cerebral blood flow.

PET studies of Alzheimer’s disease patients (compared with normal volunteers) established that: (1) glucose metabolism in the brain falls in relation to dementia severity and that parts of the brain that are most pathologically affected by disease have less glucose metabolism than less affected areas; (2) in subjects with only a memory decline (“possible” Alzheimer’s disease), a reduction in cortical glucose metabolism can be identified before the appearance of a deficit in the cognitive function that depends on that region, and indeed it will predict the

forthcoming appearance of that deficit. These studies established that metabolic and flow changes can be more sensitive markers of Alzheimer's disease than abnormal cognitive test scores.

Stressing the brain by stimulation of varying intensity while measuring cerebral blood flow with PET or functional MRI was introduced in the 1990s in order to make an early diagnosis and to directly evaluate the degree to which nerve-to-nerve communication was disturbed in Alzheimer's disease. In a PET study in which subjects were exposed to flashing lights at frequencies of 0 (dark) to 16 Hz, high-frequency-responding, high-energy-demanding synapses were shown to fail in mildly demented patients, whereas less sensitive low-frequency responding synapses failed as well in moderate to severe dementia. In a functional MRI study, cerebral blood flow responses were shown to be abnormal in genetically at-risk nondemented subjects performing a memory task.

Structural brain imaging

Two important inventions promoted the use of structural brain imaging in Alzheimer's disease: CT in the 1970s and MRI in the 1980s. When first used, CT helped to distinguish structural changes in Alzheimer's disease from changes in other illnesses that might cause dementia (e.g., tumor, stroke, normal pressure hydrocephalus, Pick disease). Later, with the help of computerized tissue categorization methods, CT was employed to show dementia-severity-related differences in net brain and gray matter volume. More recently, MRI has demonstrated regional tissue loss in subjects with "mild cognitive impairment."

Altered chemical compounds

Scanning by a process involving spectroscopy (MRS) has demonstrated abnormal concentrations of certain metabolic compounds in the Alzheimer's disease brain, consistent with disturbed metabolism and cell membrane instability. For example, abnormal phosphate compounds were noted in Alzheimer's disease brains through MRS.

White matter hyperintensities and vascular risk factors

In the 1980s, clinicians began noticing abnormal white matter areas on structural scans of the Alzheimer's disease brain. Postmortem comparisons showed that these areas represented vascular pathology and occurred in 20 to 40 percent of patients having Alzheimer's disease plaques and tangles. The areas are more frequent in Alzheimer's disease patients with risk factors such as hypertension and a high blood concentration of an amino acid called homocysteine. Too much homocysteine is related to a higher risk of coronary heart disease, stroke, and peripheral vascular disease and likely reflects the presence of a "mixed" dementia with components of both vascular-induced dementia and Alzheimer's disease. The presence of risk factors for vascular disease predicts a more rapid progression of dementia.

Familial Factors and Genes in Alzheimer's Disease

In the 1980s, family studies demonstrated that the “cumulative risk” over time of developing Alzheimer's disease, compared to the cumulative risk in the general population, was increased if a first-degree relative (parent or sibling) was affected and, to a lesser extent, if a second-degree relative had Alzheimer's disease. These studies established the importance of genetic factors in patients with familial Alzheimer's disease and provoked a search for relevant gene mutations and other genetic risk factors.

Mutations of APP, PS-1, and PS-2 contribute to familial Alzheimer's disease

In the early 1990s, a mutation of the amyloid precursor protein (APP) gene was the first to be linked to familial Alzheimer's disease. Since then, additional mutations of the APP gene, which is found on chromosome 21, have been identified, accounting for 10 percent of familial Alzheimer's disease subjects. Later linkage studies showed that mutations of genes coding for the presenilin proteins PS-1 and PS-2, found on chromosome 14 and chromosome 1, respectively, also are strongly positive for familial Alzheimer's disease. PS-1 binds with an enzyme that is believed to induce amyloid peptide plaques in brain tissue.

Genetically modified mouse models

Comparative anatomical studies showed that the regions in the brain “association system” that are most affected by Alzheimer's disease pathology expanded and differentiated rapidly during primate evolution—particularly during human evolution. This may be why no satisfactory natural animal model for Alzheimer's disease has been found.

In order to understand molecular disease mechanisms and to develop targeted drugs for Alzheimer's disease, researchers learned to microinject human genes with pathological DNA or their complementary “transgenes” into fertilized ova of mice, thus producing genetically modified mice. In the mid 1990s, a mouse model was developed with high levels of human mutant APP. Another was shown to have age-related learning impairment, in addition to plaque formation and loss of the dendrites that bring information to the cell. Feeding this mouse the nutritionally essential polyunsaturated fatty acid, docosahexaenoic acid, reduced both amyloid accumulation and dendrite loss. In another genetically modified mouse, nonsteroidal anti-inflammatory drugs lowered plaque accumulation, possibly by inhibiting an enzyme that promotes amyloid formation.

In yet another model, loss of nerve-to-nerve connections and amyloid accumulation occurred prior to plaque and neurofibrillary tangle formation. This particular sequence of changes is considered likely to occur in the natural course of Alzheimer's disease.

Other models

Genetically manipulated lower organisms (e.g., the fruit fly *Drosophila melanogaster* and the worm *Caenorhabditis elegans*) have helped to shed light upon the role of molecular disturbances associated with gene mutations, particularly of the presenilins.

Treatment Strategies

A number of treatment strategies that were initiated over the last 30 years were directly derived from new insights into potential mechanisms of Alzheimer's disease.

1. Cognition and behavior depend on information that is transmitted from nerve to nerve, but the Alzheimer's disease brain has less of the substances it needs to complete this transmission, primarily acetylcholine. Recognizing its importance in learning and memory, the FDA has approved treatments with drugs that inhibit chemicals that destroy acetylcholine. Two inhibitory drugs that are widely used today, rivastigmine and donepezil, can slow memory decline in Alzheimer's disease patients for one year or more.
2. Memantine, which is a cognitive enhancer, also has been shown to retard cognitive decline in Alzheimer's disease patients.
3. The discovery of markers of neuroinflammation in the Alzheimer's disease brain and a reported low incidence of Alzheimer's disease in arthritis patients treated with non-steroidal anti-inflammatory drugs suggested that such drugs would be of help in Alzheimer's disease. However, controlled clinical trials with nonsteroidal anti-inflammatory drugs have not demonstrated, to date, their efficacy in diagnosed patients.
4. Other treatments undergoing consideration include immunotherapy (active and passive immunization against amyloid), and administration of antioxidants (e.g., vitamin E), ginkgo biloba, polyunsaturated fatty acids, cholesterol-lowering drugs (statins), or modulators of certain enzymes (secretases) that regulate the breakdown of APP to pathological amyloid peptide.
5. One effective treatment strategy is to reduce the influence of treatable risk factors, at least for dementia associated with brain vascular pathology. These risk factors include hypertension, diabetes, smoking, cardiovascular disease, high plasma concentrations of homocysteine and protein, hyperfibrinogenemia (elevated fibrinogen levels in the blood that are believed to cause atherosclerotic plaques), and sleep apnea.

Where Are We Today?

Research in the past three decades has clarified many of the mechanisms of Alzheimer's disease compared with healthy brain aging and other neurodegenerative diseases. We do not as yet know which therapy or combination of therapies might be most effective in preventing or treating Alzheimer's disease, but we have an idea, although incomplete, of potential molecular, synaptic, and neurochemical targets for such therapy. More work is needed to dissect changes in brain biochemistry and protein-lipid processing, and to understand how different mutations lead to Alzheimer's disease pathology and how risk factors such as the *ApoE4* allele promote such pathology. New methods involving structural and functional brain imaging, measuring cerebrospinal fluid markers, and cognitive testing should be refined to diagnose the disease in its earliest stages, as therapy to be most effective likely should be introduced as early as possible. Meanwhile, the awareness that risk factors for vascular disease can add to the risk and intensity of Alzheimer's disease should lead us to treat these factors vigorously when they are present.

CAREGIVING FOR ALZHEIMER'S DISEASE: CHALLENGES AND OPPORTUNITIES

Larry D. Wright, M.D.

Among the most disturbing and inspiring professional experiences for most practicing geriatricians are the times spent working with patients and families facing the struggles of living with Alzheimer's disease. This has certainly been true for me.

In 26 years of community-based geriatric medicine practice, I have had the privilege of working with more Alzheimer's disease (AD) patients and families than I can easily recall. But my collective impression has been indelible and very rewarding, even though the immediate impact of so many of these cases has been a strong mixture of heartbreak and inspiration. And certainly I can testify that I am a better physician for having had these experiences and, I believe, a better person. Like the families and caregivers I've known, I often have felt very inadequate and unprepared for the problems AD presents. Such is the nature of this devastating disease.

Two case vignettes (here and at the conclusion of this essay) offer contrasting experiences of Alzheimer's caregiving and illustrate some of the more tragic and successful potential scenarios for patients and families afflicted with AD or other dementias.

Mary and Ed Brown had just celebrated their fifty-third wedding anniversary when his longtime family doctor told Mary that Ed's recent forgetfulness and problems balancing the checkbook probably meant he had Alzheimer's disease. No further tests or treatment was recommended since she was told the disorder was incurable and the only medicine was not really effective but very expensive. She was told to let him live as normal a life as possible for as long as possible and that she would know when to put him in a nursing home.

The ensuing two years were marked by a very gradual decline in cognitive ability mostly obvious only to Mary and a few close friends. A son and daughter both resided at a great distance and, though very devoted to their parents, expressed doubts about the accuracy of the diagnosis, having seen only minor examples of the functional and behavioral problems their mother described.

A few embarrassing episodes with friends resulted in fewer opportunities for social activity away from home. Ed lost interest in golf and preferred to stay at home with Mary most of the time.

After two minor car accidents, the family tried to encourage Ed to quit driving, but he refused to do so, adamantly claiming the accidents were not his fault and that he was an excellent driver. He also refused to consider the couple's moving closer to the children. And though Mary realized soon thereafter that he should not be left alone, Ed objected to her leaving him with someone else, even close friends, however briefly.

At the suggestion of their pastor, the couple visited a local adult day-care center. However, Ed became very angry after Mary tried to persuade him to stay there a while without her. He vowed never to go there again. Mary began to experience sleep deprivation and soon showed increasing signs of depression. Friends encouraged her to consider placing Ed in the Alzheimer's unit of a local nursing home. His wandering and episodic agitated behavior by this time had made caring for him in the home increasingly problematic for her, as well as emotionally stressful and physically exhausting. Nonetheless she pledged never to allow him to be admitted to institutional care until he no longer recognized her.

Unfortunately, Mary's own health deteriorated, and she required hospitalization for a heart attack. While under the care of a friend at home, Ed wandered outside, fell on the steps, and suffered a hip fracture. Postoperative delirium required sedative medications, and it quickly became apparent that upon discharge from the hospital he would have to be admitted to a skilled nursing facility.

Ed's three years in the nursing home were complicated by depression, intermittent agitation, and gradual functional decline. Mary visited him frequently before the stroke but remained depressed. She became more withdrawn after he entered the facility and socially more isolated. Ed died following a stroke just short of eight years after his initial diagnosis of Alzheimer's disease. A few months after his death, Mary moved away to live near her daughter. Sadly, she related a great sense of guilt that she had been unable to adequately care for her husband and maintain his quality of life in his last years. She stated she had no sense of satisfaction from her years of full-time caregiving for Ed and instead felt that those years of personal devotion and sacrifice had been a failure.

Current Status of Caregiving for Alzheimer's Disease

One of the most common and difficult societal challenges of the twenty-first century remains that of caregiving for an aging and chronically impaired population. Post-World War II children, often referred to as "age boomers," are learning about this transforming sociological change through their own caregiving experiences with their aging parents.

With the demographic projections for the aging of the Western world, caregiving for an older family member, friend, or client will be a near universal experience. Former first lady Rosalynn Carter, whose caregiving institute in Americus, Georgia, bears her name, has stated, "There are four kinds of people in the world: Those who have been caregivers, those who are currently caregivers, those who will be caregivers in the future, and those who will need caregivers."

Demographics

In the United States, about 4.5 million persons over age 65 currently living in the community are dependent on others for some type of help due to functional decline in self-care. An older adult who requires assistance with one or more activities of daily living (ADLs) is considered to be in need of long-term care (LTC) in the home. Another 1.6 million women and men require LTC in a nursing home. Approximately 21 percent of community-dwelling older persons who require LTC in the home need help with three or more ADLs.

Throughout the world the greatest growth will be among the over 85-year-olds, who will also represent the cohort with the greatest dependency and caregiving needs. The number of persons in this age group is predicted to increase from 4.2 million in 2001 to almost 21 million by 2050. Significantly, this is also the age group from which the dementia epidemic presents staggering numbers of cognitively impaired patients to the U.S. health care and social service systems.

The broad array of issues arising as part of elder care is dramatically accentuated and compounded in the typical caregiving scenarios occurring during the course of progressive functional decline in individuals afflicted with Alzheimer's disease and other memory disorders. Communicating with the cognitively impaired and the challenges of behavioral management call for extraordinary skills that most caregivers are unlikely to possess.

Caregivers on the front Lines

The history and current status of caring for dementia patients is the all-too-familiar story of courage, determination, and survival for families dedicated to preserving the dignity of their loved ones even as the most important attributes of personhood are lost. Over the last three decades, much progress has indeed been made toward improving the caregiver's preparation for the daily demands of a battle that too often feels overwhelming and unwinnable. Building on the seminal work of Nancy Mace and Peter Rabins, *The 36-Hour Day*, which became the guidebook for families of AD victims, the movement to provide information, support, and resources to families has resulted in an enormous literature of comprehensive and extremely helpful educational materials.

And while progress from scientific research has led to significant diagnostic and therapeutic advances in the medical management of Alzheimer's and other dementias, corresponding improvements in caregiving have not appeared as direct results. Instead, the prospects for improvement in the lives of caregivers have rested largely on the dissemination of educational resources and access to professionals who provide elements of counseling and care management to families and caregivers. Invariably the willingness of caregivers to accept such assistance, influenced heavily by their emotional status and degree of caregiver stress, will be a critical factor in determining benefit from this important help.

Family members as caregivers

Approximately 75 percent of in-home care of individuals with AD in the United States is provided by unpaid family caregivers, termed the informal caregiver workforce. One report places their number at 44.4 million, which represents 21 percent of the adult population. Studies have estimated their economic contribution to be as high as \$196 billion annually.

Not surprisingly, the profile of caregivers for the aged has not changed significantly from studies of 35 years ago. Most caregivers are still family members and usually women. Typically, wives, daughters, and daughters-in-law act as primary caregivers. Spouse caregivers are usually older adults who may have health problems of their own. The younger generation of family caregivers, now mostly middle-aged children, the so-called sandwich generation, are caught between responsibilities to their children and to older family members.

The informal caregiver pool is projected to decline over the coming decades, mostly attributable to changing roles of women and the transformation of the American family. The fall in the birth rate and the trend to delay childbirth or remain childless will decrease the numbers of potential caregivers. The typical baby-boomer couple today has more living parents than children. Divorce, remarriage, and geographic mobility fragment families and alter traditional filial expectations. The number of family caregivers will continue to diminish and further strain those already providing care, threatening the sustainability of the caregiving workforce balance.

Paid caregivers

Paid caregivers, whether working in the home or on staff of a nursing facility, are also usually women, mostly between the ages of 25 and 50. These direct-care workers or paraprofessional caregivers are very low paid and often inadequately trained, especially for meeting the needs of the cognitively impaired patient. Lack of benefits and the erratic, often part-time employment for this type of in-home caregiving job further contributes to a shrinking pool of workers. Formal training of in-home direct-care workers enlisted to care for older adults with Alzheimer's disease is almost nonexistent. The development of skills to deal with behavioral and communication challenges of cognitively impaired older persons has been almost totally neglected in the American health care system.

Despite current shortages, the need for paid caregivers for nursing homes and in-home settings is expected to continue to increase while the pool of entry-level workers is expected to decline by 4 percent from 2003 to 2010.

Plight of the Caregiver: Uncommon Devotion and Endless Stress

The role of primary caregiver for a dependent aged family member is among the most stressful of life situations. Even a superficial consideration of the life-changing implications of taking on this daunting responsibility confirm this claim. The days are long. The work is stressful and often lonely. And the duration of service is indefinite, possibly exceeding the caregiver's own life expectancy.

Studies have shown that providing care for a person with Alzheimer's disease is more demanding than caring for someone with physical problems alone. Round-the-clock responsibility for family matters that formerly fell to the disabled loved one, loneliness, lack of companionship, sleep deprivation, difficulty communicating with the loved one, and unpredictable behaviors that present in the mid to later stages of the disease are overwhelming. Still, health promotion and maintenance of the family caregiver—particularly efforts to avoid depression, sleep deprivation, and inadequate nutrition, as well as keeping up social and physical activities—typically are not held as priorities, especially in the early stages of the disease when it should be most important to establish these habits.

The family caregiver burden is reflected in the need for long-distance caregiving, frequently in the form of decision-making and care coordination by adult children who do not reside in close proximity to older parents with

care needs. Side effects often include (but are not limited to) strain on familial relationships and absenteeism from work and family responsibilities when travel is required plus the associated personal expenses. Geriatric care management services are uniquely equipped to assist with this type of need but are often not readily available.

The well-being of caregivers is dependent on a healthy counterbalancing of a positive attitude and a basic understanding of the Alzheimer's disease process. When caregivers are provided with sufficient information regarding the typical trajectory of the dementia, they can often prepare their responses to anticipated stages, problems, and complications of the disease. When family caregivers maintain this broader view of the progression of the disease, they are better able to accept realistically the ultimate outcome. They are also more likely to seek and accept the assistance they need to meet the ever-increasing caregiving demands.

The older caregiver is particularly burdened. The role of primary caregiver typically falls to the spouse, who may also be suffering from chronic disease and age-related health vulnerabilities. Chief among these is a general physical and psychological vulnerability to stress, which is a prominent and unavoidable feature of the caregiving role.

For all of these reasons, the first rule of caregiving is that *care of the caregiver* is the most effective treatment for the person with Alzheimer's disease. This must be communicated to the family very early on, preferably at the time of first diagnosis, and it should be repeated often. Until this message is fully understood and embraced by the whole family, especially the primary caregiver, the effectiveness of the plan of care will be compromised, and the patient will suffer even more pain and complications.

Physical and Emotional Burdens of Caregiving

The well-recognized physical and mental fatigue experienced by the family caregiver threatens the sustainability of the home-care setting for the dependent older adult. The elements at play are many and variable in their subtlety and potential, and apply whether the care-receiving older adult suffers primarily from physical disability or cognitive impairment.

For both spouse and other caregiving family members, burnout can be the eventual undoing of an otherwise stable living arrangement for the patient. The risk of caregiver stress leading to caregiver burnout is probably greater, and less often avoided, than one might expect in view of the wealth of information available on this subject. Fatigue, sleep deprivation, depression, and physical exhaustion are steps on the pathway to functional paralysis of the caregiver.

The ultimate tragedy is the fulfillment of the caregiver's worst fears—that the loved one will be institutionalized, with the concomitant sense of failure and inadequacy that often counteracts any sense of gratification and satisfaction in a job well done. One also encounters the ironic but all-too-common result of the caregiver's

sacrificial devotion: rapid decline of the health of the caregiver, resulting in the need for institutional LTC for the disabled care recipient. Frequently, this course occurs even when the caregiver's prior health history has been remarkably free of problems. And extreme caregiver stress and its complications are not limited to the spouse caregiver. Thus the tragic toll of unrelenting stress is realized in its multiplier effect on the family and the informal caregiver friends of the chronically ill.

Sleep deprivation, a very frequent feature of the caregiving experience, and its resultant energy depletion lead to increasing stress and caregiver burden. Ineffective sleep is a common symptom of clinical depression, for which the caregiver is at high risk. At other times, insomnia may actually be a causative factor that leads to depression. Clearly this is a symptom that should be addressed by the caregiver's physician as early as possible.

The probability for decline in the caregiver's own health has prompted professional counselors and educators to emphasize the importance of self-care and prevention. The message that must be driven home at every stage of the caregiving process is "You must take good care of yourself." Advice typically includes a prescription for an active lifestyle that maintains high levels of physical, mental, and social activity. In fact, for the older caregiving adult, the absence of such a healthy lifestyle must be viewed as a recipe for progressive health problems and even frailty.

The insidious nature of increasing burden over the course of a chronic disabling disease often accounts for the caregiver's overestimation of her ability to cope. In the case of gradual functional decline and dependency, caregiving efforts initially tend to be concentrated on providing assistance with instrumental activities of daily living (IADLs), which call for more nonphysical care. Only later does the care recipient's decline require help with more basic ADLs such as bathing, dressing, eating, and other more physical caregiving assistance. Indeed, one of the most important decisions in meeting the caregiving needs of the disabled older adult in the home is when to enlist a hired caregiver to supplement efforts of family caregivers. Too often this is viewed as a last resort to keep the loved one out of a nursing home; a decision for formal caregiving assistance made earlier can typically offer significant practical and personal health benefits for both the family caregiver and the care recipient.

Special Aspects of Caregiving for Older Patients With Alzheimer's Disease

Provision of information to caregivers on the natural course of the disease can be very helpful in their quest to cope with the relentless demands of life with a dementia patient. Awareness and recognition of the likely problems to be faced in the course of AD will better prepare the family and caregiver to address them and to ease any negative reactions from the loved one.

Progression of AD

Early problems in persons with AD tend to result from forgetfulness, confusion, difficulty with social conversation, personality changes, denial, and decline in executive function, or IADLs. Armed with simple skills for positive personal interactions with the loved one, such as reassurance and redirecting attention, caregivers can effectively prevent frustration from becoming a stressful situation.

Not as readily noticed at this stage is a slowing of responses, which makes driving a car dangerous. This risk will invariably progress over the course of AD and should be dealt with as early as possible to avoid both tragic consequences and the associated worry for the caregiver. Professional advice regarding driving cessation should be provided in this early stage. As the disease progresses, growing inattention to personal hygiene and other neglect appear. The AD patient may exhibit anxiety, repetitiveness, wandering, and sleeplessness. Later on, combativeness, agitation, hallucinations, delusions, verbal abuse, and, occasionally, physical threatening may develop.

For the family caregiver, the diminishing quality of the personal relationship with the loved one begins early and progresses. Particularly difficult aspects are the loneliness that accompanies the loss of companionship and the eventual loss of sexual intimacy. Compounding the deteriorating marital relationship is a decline in social activities with other couples and groups. Typically this takes a greater toll on the caregiver than on the individual with AD, although it almost always represents an undesirable loss of outside socialization for both.

As the care recipient withdraws from routines such as caretaking of the home or loses proficiency in his abilities such as tending to family finances, the spouse or other family caregiver must take on still more responsibilities. Not surprisingly, a rising sense of inadequacy often begins quite early for the caregiver, whose growing list of duties now includes areas she likely feels much less prepared to handle. This is frequently made worse by the loved one's unwillingness to relinquish tasks he can no longer reliably complete.

Probably the most stressful challenge for most Alzheimer's caregivers is dealing with the distressing and sometimes frightening behaviors that can arise during the middle and late stages of the disease. Such neuropsychiatric symptoms are reported to occur in more than 80 percent of subjects in studies of AD.

Irritation, anger, and even rage reactions are commonly encountered aggressive behaviors. Even more disturbing are the possible psychoses: hallucinations, delusions, suspiciousness, and paranoia. Wandering and aggressive sexual behavior, also manifestations of the disease at this stage, require vigilance and close management. Dealing

with these behaviors represents a breaking point that stretches caregivers beyond their ability to cope well. For this reason in particular it is critical that effective management strategies be developed for the AD patient.

Most caregivers need professional assistance and counseling from physicians, psychologists, geriatric psychiatrists, and social workers to deal with these problem behaviors. A rational and successful approach is a professional review of the observations documented by the caregivers in order to identify a predictable pattern based on a recurring sequence of events. If most episodes follow a typical pattern with predictable triggers and expected outcomes, caregivers can be coached in how to effectively arrest the process and avoid escalation of the behavior.

Other interventions that can alleviate or inhibit these behaviors include playing music, showing videotapes of family members, playing audiotapes of voices of caregivers or family members, encouraging light physical exercise, and providing sensory stimulation and relaxation techniques. Such nonpharmacological interventions should be tried first to avoid the risk of adverse effects and the additional expense of drugs. Nonetheless, AD patients often require psychotropic medications for satisfactory management of many of the distressing symptoms. Thus, a multifaceted response to this period of troublesome behaviors may restore some measure of control and hopefully restore the caregiver's ability to cope.

For physicians and other professionals who work with AD patients, early grieving by the spouse or family caregivers is so common as to be thought of as virtually a universal aspect of caregiving for Alzheimer's. These caregivers experience particularly high levels of distress and depression that may not resolve completely until after the loved one's death. However, it is commonly observed that the Alzheimer's caregiver experiences significantly less intense negative effects of bereavement following the death, resulting in earlier adaptive functioning and recovery. Only about 20 percent of Alzheimer's caregivers experience intense grief and depression following the loved one's death.

There is great variability among caregivers for AD in their ability to keep the patient at home through the complete course of the disease. While many caregivers are fortunate to be able to maintain an AD patient at home, more will eventually have to move their loved one into a facility. This may be a memory-care unit that operates as an assisted-living facility (ALF) or more likely an LTC facility, due to the need for special medications, supervision, and care by nurses.

Finances

The financial burdens of Alzheimer's care whether in the home, especially when hired caregiving is required, or in a facility (ALF or LTC) are often great. Obtaining professional financial planning and advice can ensure that the family is aware of all available sources of possible funds for which the patient might qualify.

As early as possible after the diagnosis, the Alzheimer's patient should establish advance directives such as a living will and the appointment of a proxy or surrogate decision-maker for health decisions. Mild stages of cognitive impairment do not necessarily result in the loss of mental capacity that would legally preclude such autonomous personal decision-making by the individual, but such capacity will be lost at some point as the

disease progresses. Although in many states prevailing laws allow designation of a proxy as well as the creation of a living will without the assistance and expense of an attorney, the most helpful such proxy document, the Durable Power of Attorney for Health Care, does depend on such legal services. Consideration of legal guardianship for the Alzheimer's victim is often needed in the later stages and, for this reason, early discussion of this process with an attorney can help the family plan its care management.

Early exploration of medical treatment preferences for end of life, including palliative care and ultimately hospice care, is also advisable. Under such plan of care it is determined that aggressive treatment for symptom relief and pursuit of comfort measures become the primary goals of care while medical intervention to prolong life is no longer desirable. At what point such a care plan is adopted is a very personal and, at times, difficult decision. If done early enough, meaningful input by the individual with AD can be very instructive and bring family consensus around such decisions. This type of planning can prevent painful family conflicts and indecision later.

Resources for Caregiving with Alzheimer's Disease

Families dealing with Alzheimer's disease or other dementias will need many different community resources and services as the disease progresses. Because availability and organization of specific services and support varies with communities, knowledge and familiarity of the array of health care and social services in one's own community is important to acquire early. Generally these resources include health care, information, and education for the caregiver and respite-care referrals.

Access to geriatric care management services, information, and programs, often provided by community organizations or private consultation through social workers or nurses, is very helpful to patients and families dealing with dementia. One of the most useful sources is the Alzheimer's Association, which essentially serves as a clearing-house for information, resources, and educational materials. At any stage of the disease, this organization serves as the caregiver's most consistent resource for accessing the network of dementia information and services of all types.

Primary care medical services can be provided by geriatricians, internists, or family practitioners who have experience and interest in the care of older adults and in dementia. Geriatricians are trained to manage the complex needs of older adults and can evaluate and address the medical, functional, and behavioral issues affecting both the patient and the caregiver. Moreover, they typically work as part of interdisciplinary teams of nurses, social workers, nurse practitioners, and other health professionals with additional training or experience in the care of older patients.

Geriatric psychiatrists, neuropsychologists, and neurologists are among the specialists who can manage patients with AD and other dementias. Consultations at the first suspicion of cognitive impairment can ensure definitive diagnosis at the earliest point possible. Memory-disorder centers, more commonplace among com-

munity-based services in recent years, are excellent resources for evaluation and treatment recommendations to families and physicians dealing with cognitive dysfunction in patients.

Respite-care services include adult day-care centers as well as ALF and LTC facilities. Families and caregivers must be encouraged to utilize these services despite frequently encountered resistance from the AD patient. Respite services, though typically underutilized, can be critically important to sustaining the health and functional role of the caregiver in the home.

There is a shortage of in-home, direct-care workers in most communities in this country, and most of those available, whether private contractors or agency employees, have inadequate training. Nonetheless, in order to maintain an AD patient in the home setting as the disease progresses, hiring such caregivers is usually required to supplement the efforts of the family caregiver. The extent of help needed is likely to increase as the care recipient's dependency and needs heighten over time.

Ultimately, many AD patients will require institutional care despite all the best efforts of family and caregivers to maintain them in the home setting. Typically it is the problem of difficult behaviors that cannot be adequately managed at home or the declining health of the primary family caregiver that determines the need for this transfer of settings. Ideally when this occurs, ALFs or LTC facilities that have developed special units for dementia care will be available. Typically staffs in these units have substantial additional training and experience in dealing with the behavior problems associated with Alzheimer's and other dementias.

Other worthwhile services include caregiver education, training, and support groups. Elder-law attorneys and financial planners with experience in advising families of AD patients are important resources that should be utilized.

Finding Meaning and Personal Growth Despite Great Loss: Positive Aspects of the Caregiving Experience

It is abundantly clear that the journey of caregiving is fraught with great risks for complications and failure, especially with respect to one's personal health and well-being. Struggle is a common denominator. But there are also many examples of personal triumph and success among family caregivers who have found ways to overcome tragic circumstance, meet the continual demands of caregiving, and realize great meaning from the experience.

Not surprisingly, a cornerstone of this type of exceptional personal achievement is maintenance of a healthy and active lifestyle, with an emphasis on activities that are energy repleting. These include aerobic exercise such as walking, swimming, and bicycling; creative endeavors such as art, music, and writing; positive

social/recreational activities such as bridge, book clubs, and faith-based activities, as well as volunteer work. Other aspects of a healthy lifestyle include good nutrition, stress management, and social engagement. Holistic body-mind health also appears to be a common trait. Giving oneself permission to accept and ask for help is also affirming, as is retaining some important areas of personal involvement in select groups or community activity. These and other related endeavors may serve to counter the strong feelings of isolation, loss, sadness, anger, and resentment that can lead to depression.

Taking private time as well should be consistent and protected. Similarly, identifying available resources for respite and utilizing these on some periodic schedule can be a most helpful way of refreshing and maintaining one's physical and psychological reserves for coping with the continual stresses of caregiving. Even travel, whether short trips (overnight or weekends) or the occasional longer vacation planned well in advance (especially in the later stages of AD), can be an extremely useful way of recharging one's batteries for the long course of Alzheimer's caregiving.

Although the path to greater meaning during the caregiver experience is variable and personal, there are a number of keys to finding this preferred way of living. The following is a representative, though certainly not exhaustive, list of activities that many family caregivers have found to be instrumental in discovering and preserving personal meaning throughout the caregiving experience. They often will be sources of energy renewal amid the constant demands that otherwise rob life-sustaining energy.

1. ***Pursue at least one area of personal creativity.*** The possibilities for fulfilling creative expression are endless. Which specific activity is most rewarding will vary widely depending on the individual's background, interests, talents, and personality. Music, the visual arts, and poetry are obvious examples of creative expression, but gardening, woodworking, mentoring, writing, and studying a new subject serve this purpose as well. Such endeavors, whether an established, familiar interest or a completely new pursuit, bring personal satisfaction and growth.
2. ***Celebrate the life of the loved one with Alzheimer's.*** Write the life story or record significant memories or accomplishments in a form that celebrates a life's legacy to be shared with others. Incorporating the individual's own life review, which is often rich with vividly recollected memories in the early and even the mid stages of AD, is a meaningful project. A scrapbook, photo album, or publishable memoir can serve the important purpose of ensuring that family, friends, caregivers, or those who never knew the person before AD have the opportunity to understand who she really is and what her life has been.

3. ***Practice journaling during the caregiving experience.*** Keeping a personal record of one's life is a powerful way of finding meaning even through painful experiences. The discipline of writing causes one to step back from the difficulties of the caregiving role and reflect on personal thoughts, feelings, disappointments, hopes, and desires. Intentional reflection often results in surprising insights and comfort for someone faced with the continual stresses of caregiving, and it can be a useful way of dealing with the grief that often begins early in the course of AD.
4. ***Include meditation or other spiritual practices in the daily routine.*** Any of the traditional spiritual disciplines, but especially meditation and prayer, have been shown to strengthen one's inner reserves for coping with the stresses of caregiving. Even among people who do not consider themselves religious, there is often recognition of their own spiritual nature and resources for inner strength. Scheduling regular times for quiet and solitude creates great opportunity for spiritual growth. Those who pursue this path, and are able to make it an integral part of the caregiving journey, often report discovering a deeper spirituality as the most rewarding aspect of the caregiving experience.
5. ***Find someone to talk with on a regular basis.*** Have at least one confidante with whom to openly and safely share thoughts, feelings, difficulties, and joys. Though a very close friend or family member can provide this kind of special relationship, often clergy or a professional counselor can be even more helpful, especially when additional issues complicate the usual stresses of caregiving. The person's most important attributes include being a good listener who brings unconditional acceptance and support, along with honest, caring feedback.

Caregivers who have found sources of greater meaning during the caregiving experience often have smoother transitions into their post-caregiving roles after the death of a loved one to AD. Moreover, those who have found the more positive caregiver experiences typically are better prepared to help others faced with the same types of caregiving challenges. In fact, former AD caregivers are often most effective in later roles as "wounded healers," counseling and supporting other family caregivers, through volunteer participation, in support groups or in one-on-one counseling. Such service to others can be the culmination of the individual's own quest to find meaning from life's most painful of ordeals.

A Vision for Coordination of Services in Support of Alzheimer's Caregiving

Too often the greatest barrier to healthy caregiving for families of individuals with memory disorders is lack of ready availability of community-based medical, mental health, social, and support services. And even when needed services exist, the lack of coordination of programs and services makes accessibility unnecessarily difficult. The continuum of care for services and support resources to patients and families with dementia is seldom comprehensive and usually fragmented.

A locally based system that is developed to create a functional network serving as the coordination point for the care continuum of memory-disorder services is the ideal goal for every community. Such a system would include professional services of a community mental health center and geriatricians, as well as the full interdisciplinary array of clinical professionals. Ideally primary care physicians, neurologists, neuropsychologists, and geriatric psychiatrists would be directly linked within this closely connected network with a core team of geriatric case managers, social workers, nurses, nurse practitioners, and pharmacists. Ready access to other medical specialists and services would allow efficient referrals of patients and families for additional evaluation and treatment where appropriate.

Closely linked community-based services would include adult day programs, support groups, caregiver training/support programs, home health care, respite services, and residential facilities such as assisted living, memory-care units, skilled nursing, and long-term care. Hospice home care and inpatient services would be an integral part as well.

The team approach proceeds from a comprehensive geriatric assessment that is multidisciplinary and informed by all the clinical, psychological, and social factors identified in each case. From this baseline understanding of the risks and realities, a plan of care addressing the needs of all those affected by the disease—patient, family, and caregivers—can be conscientiously developed.

The coordinating hub of this model of community services would be a memory resource center providing readily available advice, information, education, and support of families and caregivers. It would also serve as an entry point for families and patients seeking help with suspected memory-loss problems prior to diagnosis. Widely available educational resources for initial training and continuing education of informal and formal caregivers of patients with cognitive problems could be found here, as well as referrals to other community resources.

In this model the patient and family participate with the clinical team in charting a plan of care that honors their values and goals, empowering them to use all their energies in pursuit of efforts that provide the best

possible caregiving while also preserving the mental and physical health of all those affected.

This type of service coordination provides the optimum support for patients and families facing the many challenges of living with memory loss. It eliminates the risk of isolation from the community and instead allows caregivers to be more effective in their roles and to cope in healthy ways.

A comprehensive system of services, intentionally patient- and family-centered, would serve to empower families and caregivers of AD victims. Every community with substantial medical, mental health, and social services has the potential to form this type of coordinated community services for families afflicted with memory disorders. The challenge is in articulating a vision that can inspire the community to organize for optimal delivery of these services to those who need and deserve this kind of help.

Even at this time in history, while there is no cure or satisfactory medical treatment for Alzheimer's disease, there is much known about how to provide quality care to patients, families, and caregivers. If the American system of health care and social services makes sufficient commitment to delivering this type of care, the families of AD patients can know their loved ones will receive competent, compassionate care that preserves their dignity while protecting the health or well-being of their caregivers.

A final case vignette offers a contrasting experience of family and caregivers responding to the challenges of Alzheimer's disease.

Katherine Collins reported her concern about the difficulty she had noticed in remembering appointments to her internist at the time of her regular checkup. Even though her score on a mini mental-state exam was technically acceptable at 27 of possible 30, the doctor was concerned and referred her to a neuropsychologist at the Memory Disorder Center in their community. The three-hour evaluation resulted in a diagnosis of mild cognitive impairment (MCI), and when her performance showed further decline on a repeat evaluation six months later, she was placed on a cholinesterase inhibitor medication for the likelihood that her MCI represented a precursor to Alzheimer's disease. In fact, though she continued to function at a high level of independence, over the ensuing two years she progressed to a certain diagnosis of AD.

Katherine's husband, Joe, at 79 was two years older but in generally excellent health. Fortunately Katherine required little physical care, though she gradually grew more dependent on her husband in all IADLs and executive functions. She gave up driving on the advice of her doctor and family at age 78 but remained socially and physically active. Joe embraced a very active lifestyle including daily three-mile walks, weekly golf, and tai chi at least three days a week. He enlisted friends early in the course of Katherine's illness to stay with her for a few hours at a time, and she grew accustomed to his not always being there.

Gradually, Katherine became more dependent in basic ADLs, needing assistance with bathing, dressing, and grooming. Seven years after the original diagnosis of MCI, she began to show some tendency to wander outside the house, and thereafter required constant attendance. At that point, Joe began taking her to a local adult day-care center, initially three days a week and increasing to five days a week over the ensuing year. Hired caregivers gave additional respite for Joe about eight hours a week, and with urging of his family, physician, and geriatric-care manager, he was able to maintain his active lifestyle. Joe protected his personal time as much as possible but began to spend much of it learning to use the personal computer his son had given him. He developed new areas of learning through online research, but mostly he used it to write Katherine's life history to share with her family and friends as well as those new caregivers who knew nothing of her life and legacy.

At the insistence of his son who resided at a great distance in another state, Joe placed Katherine briefly in respite care in a memory-care unit while he made one-week trips to attend the college graduation of a grandson and the wedding of a granddaughter. By this time Katherine, nine years post-original diagnosis, no longer was able to call him by name and did not enjoy outings in the car any longer. She could not make the trips herself, but Joe took the biography he had completed and the scrapbook of photographs and other memories to share and celebrate her life and legacy with extended family.

Fortunately, Joe successfully avoided depression and maintained a very high level of personal health through the caregiving experience. When Katherine, at age 85, required permanent residence in the memory-care unit, Joe visited her daily. The next year Katherine suffered a heart attack and remained in congestive heart failure until her death in hospice three months later. Joe was at her bedside when she died and expressed gratitude that she had never suffered or required admission to a hospital at any time during her 11-year course with dementia. That's the way she said she wanted it.

Joe stated that he had grieved long before Katherine's death, during the early years when he truly recognized he was losing the person he knew so well to Alzheimer's disease. He expressed gratitude for the support they had received at every stage of her disease and the difference the friends, family, hired caregivers, and respite services had made in allowing him to maintain his physical and mental health, ensuring that most of the time he had with Katherine was quality time.

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